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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KUBELIK, ANNE R

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/519,820	Applicant(s) DANIELL, HENRY	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2008 and 21 July 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 and 32-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 and 32-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-21, 28-30 and 32-34 are pending.
2. The objection to claims 33-34 to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only is withdrawn in light of Applicant's amendment of the claims.
3. Claims 1-8, 14-16, 19-21, 28 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hajukiewicz et al (WO 00/03022) in view of Goodman et al (1997, US Patent 5,629,175) is withdrawn in light of Applicant's amendments to claim 1.

Claim Objections

4. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 fails to further limit claim 1 because it recites no structure that enables expression in a chloroplast but not other types of plastids. The objection is repeated for the reasons of record as set forth in the Office action mailed 7 August 2008. Applicant's arguments filed 8 December 2008 have been fully considered but they are not persuasive.

Applicant urges that the claims have been amended to address this issue (response pg 8).

This is not found persuasive because the amendment does not recites a structure that enables expression in a chloroplast but not other types of plastids.

Claim Rejections - 35 USC § 112

5. Claims 3 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 7 August 2008, due to Applicant's amendment of the claim. Applicant's arguments filed 8 December 2008 have been fully considered but they do not apply to this new rejection.

Claim 3 lacks antecedent basis for the limitation "the plastid".

Claim 13 is indefinite in its recitation of the limitation "the IGF-1 is inserted into an inverted repeat region of the plastid genome" makes no sense when talking about a vector.

Claim Rejections - 35 USC § 103

6. Claims 1-16, 19-21, 28 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hajukiewicz et al (WO 00/03022) in view of Goodman et al (1997, US Patent 5,629,175) and further in view of Daniell (WO 99/10513). The rejection is repeated for the reasons of record as set forth in the Office action mailed 7 August 2008. Applicant's arguments filed 8 December 2008 have been fully considered but they are not persuasive.

The claims are drawn to a plastid transformation vector comprising a first flanking sequence, a DNA encoding insulin-like growth factor (IFG-1), and a second flanking sequence, wherein the DNA is operably linked to the psbA 5' UTR and 3'UTR, wherein the flanking sequences are sequences in a spacer region. The claims are also drawn to an edible plant transformed with the vector.

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Hajukiewicz et al teach transformation of tobacco chloroplasts (pg 27-, line 22, to pg 29, line 19) with vectors comprising an expression cassette comprising the psbA 5' promoter, a sequence encoding a mammalian protein, human growth hormone, the aadA selection marker, and the psbA 3' UTR terminator, wherein the cassettes is flanked by plastid sequences that target the expression cassette upstream of the plastid 16S rDNA (pg 25, line 24, to pg 26, line 5) to transplastomic tobacco plants that express bioactive human growth hormone at high levels (pg 42, line 20, to pg 47, line 17). Tobacco would be suitable for consumption by a mammal of one species or another.

Hajukiewicz et al do not teach expression of insulin-like growth factor in tobacco plastids and do not teach sequences in a spacer region as the flanking sequences.

Goodman et al teach expression of mammalian proteins, including insulin-like growth factor, in plants (column 3, lines 11-29).

Daniell teach a plastid transformation vector that can be used to transform the chloroplasts of a wide variety of plant species (pg 9, line 1, to pg 12, line 14; pg 20, line 4, to pg 27, line 6); the vector uses trnI and trnA, which correspond to a transcriptionally active spacer region, as the flanking sequences.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of expressing a mammalian protein in tobacco plastids as taught by Hajukiewicz et al to use the insulin-like growth factor as the mammalian protein, as described in Goodman et al. One of ordinary skill in the art would have been motivated to do so because substitution of one desirable and economically important mammalian protein for another is an obvious design choice.

At the time the invention was made, it also would have been obvious to one of ordinary skill in the art to use trnI and trnA as the flanking sequences as described in Daniell. One of ordinary skill in the art would have been motivated to do so because of the advantages of these flanking sequences in expressing proteins, especially high value ones, in a wide variety of plants species (Daniell, pg 8, lines 2-10).

One of ordinary skill in the art would have been motivated to optimize the codon usage of the sequence encoding IGF for expression in plastids, as it is well known that proteins express better when the codons they are expressed from match the genome from which they are being expressed. Thus, absence any evidence that SEQ ID NO:2, which encodes IGF, is expressed at unexpectedly higher levels than other plastid-optimized IGF coding sequences, SEQ ID NO:2 is obvious over other the sequence of IGF.

Applicant urges Hajukiewicz et al does not teach expression of IGF in tobacco plastids and Goodman et al only teaches nuclear experssion

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

It is noted that Applicant's arguments focused only the rejection of Hajukiewicz et al (WO 00/03022) in view of Goodman et al, and did not address the rejection of claims 9-13 over Hajukiewicz et al in view of Goodman et al and further in view of Daniell.

7. Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hajukiewicz et al in view of Goodman et al and further in view of Daniell as applied to claims 1-

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16, 19-21, 28 and 32 above, and further in view of Ursin et al (1997, US Patent 5,633,153).

Applicant did not address this rejection in the response filed 8 December 2008.

The claims are drawn to a plastid transformation vector comprising a first flanking sequence, a DNA encoding insulin-like growth factor (IFG-1), and a second flanking sequence, wherein the vector further encodes BADH as a selectable marker.

The teachings of Hajukiewicz et al in view of Goodman et al and further in view of Daniell are discussed above. Hajukiewicz et al in view of Goodman et al and further in view of Daniell do not teach BADH as a selectable marker.

Ursin et al teach use of a nucleic acid encoding betaine aldehyde dehydrogenase as a selectable marker in plants (claims 1-21). The protein is targeted to the chloroplasts (column 5, lines 17-41) and the resulting plants are resistant to betaine aldehyde (column 10, lines 1-27). Ursin et al teaches that unmodified plant BADH genes were effective for selection at a wide range of betaine aldehyde concentrations (Table 3) and the effectiveness of BADH as a selectable marker in tobacco (column 8, lines 55, to column 9, line 67).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of the method of expressing insulin-like growth factor in plastids as taught by Hajukiewicz et al in view of Goodman et al to use BADH as a selectable marker as described in Ursin et al. One of ordinary skill in the art would have been motivated to do so because Ursin et al teaches the use of BADH as a selectable marker and because substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice.

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Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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October 7, 2009

/Anne R Kubelik/

Primary Examiner, Art Unit 1638